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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/020,393
Filing Date	February 9, 1998
First Named Inventor	Peter J. Sims
Group Art Unit	1644
Examiner Name	Gambel, Phillip
Total Number of Pages in This Submission	
Attorney Docket Number	OMRF 170

ENCLOSURES *(check all that apply)*

- [x] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment / Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
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- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
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- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
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- [x] Appeal Communication to Group (*Appeal Notice, Brief, Reply Brief*)
- [ ] Proprietary Information
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- [x] Other Enclosure(s) (*please identify below*):

Request for Oral Hearing; check for $140.00; return postcard

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

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Signature	
Date	June 26, 2002

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☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 140.00

Complete if Known	
Application Number	~~09/020,393~~
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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	740	201	370	Utility filing fee	
106	330	206	165	Design filing fee	
107	510	207	255	Plant filing fee	
108	740	208	370	Reissue filing fee	
114	160	214	80	Provisional filing fee	

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2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims		Fee from below		Fee Paid
Total Claims		- 20 =		X		=	
Independent Claims		- 3 =		X		=	
Multiple Dependent						=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claim, if not paid
109	84	209	42	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) .00

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105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	400	216	200	Extension for reply within second month	
117	920	217	460	Extension for reply within third month	
118	1,440	218	720	Extension for reply within fourth month	
128	1,960	228	980	Extension for reply within fifth month	
119	320	219	160	Notice of Appeal	
120	320	220	160	Filing a brief in support of an appeal	
121	280	221	140	Request for oral hearing	140.00
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,280	241	640	Petition to revive - unintentional	
142	1,280	242	640	Utility issue fee (or reissue)	
143	460	243	230	Design issue fee	
144	620	244	310	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1.17(q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	740	246	370	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	740	249	370	For each additional invention to be examined (37 CFR § 1.129(b))	
179	740	279	370	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid **SUBTOTAL (3)** ($) 140.00

SUBMITTED BY

Name (Print/Type)	Patrea L. Pabst	Registration No. (Attorney/Agent)	31,284	Telephone	(404) 817-8473
Signature				Date	June 26, 2002

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Peter J. Sims

Serial No.: 09/020,393 Art Unit: 1644

Filed: February 9, 1998 Examiner: P. Gambel

For: *COMPOSITIONS AND METHODS TO INHIBIT FORMATION OF THE C5B-9 COMPLEX OF COMPLEMENT*

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY TO EXAMINER'S ANSWER

Sir:

This is an appeal from the final rejection of claims 10-12, 16 and 17 and withdrawal of claims 1-9, 13-15, and 18-35 in the Office Action mailed January 28, 2000 in the above-identified patent application, revised in response to the Notice mailed April 17, 2001. This is a reply to the Examiner's Answer mailed April 26, 2002. A Request for Oral Hearing accompanies this Reply along with the fee for a small entity. **Please note that there has been a change in correspondence to Holland & Knight LLP, One Atlantic Center Suite 2000, 1201 W. Peachtree Street, Atlanta, GA 30309-3400.**

The following is in Reply only to those sections where new issues or differences in opinion are apparent.

(3) STATUS OF CLAIMS ON APPEAL

Claims 1-35 are pending. Claims 1-35 were restricted into thirty-two groups in an Office Action mailed February 4, 1999. This requirement was traversed and a petition

for reconsideration mailed on November 8, 1999. A Decision was mailed March 17, 2000, and received December 28, 2000. Claims 10-12, 16 and 17 were finally rejected in the Office Action mailed January 28, 2000.

(5) SUMMARY OF THE INVENTION

Compounds modulating CD59 mediated complement activity which are based on the identification of the hu CD59 amino acid residues which serve as the binding site for CD59-C9 interactions are described and claimed. These residues correspond to amino acid residues 42-58 of human CD59, and bind to the region of C9 corresponding to human C9 amino acids 334-418, more specifically, amino acid residues 359 and 384 of human C9. The claimed compounds are derived using this basic amino acid sequence, amino acid residues 42-58 of human CD59, and corresponding three dimensional structure within the protein using any of several techniques known to those skilled in the art, including rational drug design using computer data bases and modeling of peptide/protein-ligand binding, antibodies and anti-idiotypic antibodies generated to the proteins or peptides containing this peptide sequence, and modified peptides. Those compounds imitating the structure and/or function of the peptide region are referred to as "peptidomimetics", and include small molecules which present the surface exposed side chains in these amino acids in the same relative positions, compounds identified by combinatorial chemistry techniques which bind to the active portions of human C9, as well as modified peptides (page 6, line 16 to page 7, line 3), and antibodies. The antibodies must present the structure of amino acid residues 42-58 of human CD59, however, to be within the scope of the claims (see claim 10), not just bind to C9.

The compounds can be used to inhibit complement by binding to C9 analogously to CD59, or to maintain complement inhibition, by blocking CD59 binding to C9. The compounds can be administered locally or systemically in any suitable carrier in an amount effective to either inhibit complement or block the inhibition of complement, in a patient in need of treatment thereof. (page 7, lines 3-9)

The claims are drawn to a molecule mimicking the region of human CD59 which is both species specific (i.e., unique to human) (page 12, lines 7-13) and which binds to C9, thereby inhibiting complement activation mediated by formation of the human C5b-9 complex and not that of other species (page 13, lines 21-24). There is an important limitation in the claims: the compound must structurally mimick human CD59 amino acid resides 42-58 when these amino acids have the same spatial orientation as when present in the intact molecule (page 19, lines 8-16). The compound must bind specifically to amino acids 359 to 384 of human C9 (page 43, line 23 to page 45, line 13).

(6) ISSUES ON APPEAL

The issues presented on appeal are:

(1) whether claims 10-12 and 16-17 are properly rejected under 35 U.S.C. §112, second paragraph, on the basis that the claimed invention is not clearly defined in the application;

(2) whether claims 10-12 and 16-17 are properly rejected under 35 U.S.C. §112, first paragraph, on the basis that the claimed invention is not clearly enabled by the application;

(3) whether claims 10-12 and 16-17 are disclosed by under 35 U.S.C. §102(b) or obvious under 35 U.S.C. §103 over U.S. Patent No. 5,550,108 to Sims, et al.; and

(4) whether claims 10-12 and 16-17 are obvious under 35 U.S.C. §103 over the combination of U.S. patent No. 5,550,108 to Sims and Chang, et al., J. Biol. Chem.269(42), 26424-26430 (1994).

(7) GROUPING OF CLAIMS

The claims do not stand or fall together. The claims must be considered separately because they are drawn to different chemical entities - indeed this was the basis for requiring that appellant elect a single species from the species defined by claims 10-12, 16, 17, 27-29, and 33-35, which fall within the generic claim 10.

Claim 10 is drawn to a method for inhibiting human C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition comprising a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules having the structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9.

Claim 11 defines the species of peptidomimetic as a small molecule which binds specifically to amino acids 359 to 384 of human C9.

Claim 12 defines the species of peptidomimetics as an antibody.

Claim 13 defines the peptidomimetic as a chimeric peptide which includes the amino acids 42 to 58 of the human sequence of CD59. Claim 14 defines the peptidomimetics as a covalently cyclized peptide comprising human CD59 amino acid residues 42 to 58. Claim 15 defines the peptidomimetic as a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of human CD59. Claim 18 defines the peptidomimetic as comprising the side chains of human CD59 amino acid

residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the spatial orientation and alignment of hu CD59. Claim 19 defines the peptidomimetic of claim 18 wherein the spatial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are deduced by NMR structure determination.

Claims 16 and 17 are drawn to a method of treatment (claim 17) and inclusion in the composition of a pharmaceutically acceptable carrier for administration to patients in need thereof.

Accordingly, at a minimum, the claims must be examined separately based on whether or not they require further limitations as to the chemical structure of the peptidomimetic, or go to the method of use. As to the peptidomimetics, these should be examined separately for both enablement and with regard to the prior art, which does not show inhibitors as defined by the claims.

The examiner has not argued that these are all the same species, nor withdrawn the election of species requirement. If a determination is made that the elected species are patentable, this case must be remanded to the examiner for an evaluation of the patentability of the non-elected species. Indeed, as the examiner notes, his rejections under 35 U.S.C. 112, address those claims drawn to species which were **not elected**, calling into question just what claims and species are presented here on appeal, and which are properly the subject of remand and examination, notwithstanding the decision on Appellants' petition regarding this apparent inconsistency and what is still believed to be an improper restriction requirement and election of species.

(8) ARGUMENTS

(i) The Invention

The complement system and the role the claimed compounds play has been explained previously in the Appeal Brief. However, the Examiner still fails to recognize what is claimed by independent claim 10, and the claims which depend thereon:

> 10. A method for inhibiting human C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition comprising
>
> a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules
>
> having the structure and
>
> function of human CD59 amino acid residues 42-58, and
>
> binding specifically to amino acid residues 359-384 of human C9.

There is nothing confusing nor vague in this language. The amino acid sequence of human C59 amino acid residues 42-58 is explicitly provided. The structures of the individual amino acids are known and the sequence can be inputted into any of a number of computer programs to provide a three-dimensional structure. It is a compound with this structure that is claimed. It is this structure which is essential if one is to inhibit human C9.

Any compound having this structure should bind to human C9, although it is a routine matter to screen for binding and inhibition of activity, using assays that have been in use for decades. Compounds can be derived using this basic amino acid sequence and corresponding three dimensional structure within the protein using any of several

techniques known to those skilled in the art, including rational drug design using computer data bases and modeling of peptide/protein-ligand binding, antibodies and anti-idiotypic antibodies generated to the proteins or peptides containing this peptide sequence, and modified peptides. Those compounds imitating the structure and/or function of the peptide region are referred to herein as "peptidomimetics", and include small molecules which present the surface exposed side chains in these amino acids in the same relative positions, compounds identified by combinatorial chemistry techniques which bind to the active portions of human C9, as well as modified peptides.

The compounds can be used to inhibit complement by binding to C9 analogously to CD59, or to maintain complement inhibition, by blocking CD59 binding to C9. The compounds can be administered locally or systemically in any suitable carrier in an amount effective to either inhibit complement or block the inhibition of complement, in a patient in need of treatment thereof.

The application provides an extensive disclosure of the methods and materials required to make these peptidomimetics. The critical features of the CD59 and C9 which must interact to provide species specific inhibition are described in the application at pages 12-13. Chimeric proteins are described at page 13, line 26 to page 14, line 6. Antibodies to amino acids 42-58 of CD59 and antibodies to amino acids 359-384 of hu 9 are described at page 14, line 7 to page 17, line 19, and demonstrated in the examples, as discussed below. Identification of compounds by combinatorial chemical is described at pae 17, line 20 to page 18, line 26. Rational drug design and suitable computer software for use therein is described at page 18, line 27 to page 24, line 13. Methods for synthesis of these compounds are described at page 24, line 14 to page 27, line 9. Methods of

treatment are described at page 28, line 3 to page 29, line 11. The examples further demonstrate the production and testing of both specific antibodies and modified peptides that are useful in blocking binding of C9 to CD59. Specifically, example 1, at page 28, line 15 to page 39, line 30, describes making CD59 chimeric proteins which inhibit C9 binding. Example 2, at page 40, line 1 to page 43, line 22, describes making site directed mutations in C9 peptides and chimeric proteins to create inhibitors which block binding to C9/CD59. Example 2, page 43, lines 23-29, describes making antibodies to C9 peptide 359-384. The results at pages 44-48 and accompanying figures demonstrate that these peptides, chimeric proteins and antibodies were effective as specific specific complement inhibitors.

(ii) Rejections Under 35 U.S.C. § 112, first pararaph

The Court of Appeals for the Federal Circuit (CAFC) has most recently stated that to satisfy the legal standard for enablement under § 112, first paragraph, a patent application must adequately disclose the claimed invention so as to enable a person skilled in the art to practice the invention at the time the application was filed without undue experimentation. Enzo Biochem, Inc. v Calgene, Inc., 188 F.3d 1362, 1371-1372, 52 USPQ2d 1129 (Fed. Cir. 1999); accord Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997). However, "nothing more than objective enablement is required, and therefor it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). As set forth in In re Wright, 999 F.2d 1557, 1561-1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993):

> When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by the claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (M.I.T. v. A.B. Fortia, 774 F.2d 1104 (Fed. Cir. 1985)). In addition, as affirmed by the Court in Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524 (Fed. Cir. 1987), a patent need not teach, and preferably omits, what is well known in the art.

Whether making or using the invention would have required undue experimentation, and thus whether the disclosure is enabling, is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. In cases that involve unpredictable factors, "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." In re Fisher, 427

F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

> The test is not merely quantitative, since a considerable amount of experiment is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.
>
> Ex parte Jackson, 217 USPQ 804, 807 (1982)

As stated in the MANUAL OF PATENT EXAMINING PROCEDURE §2164.04 (7th ed. 1998), *citing* In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993), the examiner has the initial burden to establish a reasonable basis to question the enablement of the application.

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must be taken as being in compliance with the enablement requirement** of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.
>
> *Id.* at § 2164.05 (emphasis added).

In this case, the examiner has consistently relied on conclusory statements without putting forth specific reasons describing why the claims are not enabled by the specification. The patent examiner cannot just assert that the application is not enabled. As stated in In re Marzocchi at 439 F.2d 220 (CCPA 1971):

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made [, enablement under § 112, first paragraph], to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the Appellant to go to the trouble and expense of supporting his presumptively accurate disclosure.
>
> *Id.* at 224.

The MPEP instructs examiners to make specific findings of *facts* to rebut Appellants' presumption and "specifically identify what information is missing and why one of skill in the art could not supply the information without undue experimentation." MPEP at § 2164.05. The examiner should provide references to support a *prima facie* case of lack of enablement. *Id.*

There is no legal requirement that an inventor have actually reduced the invention to practice prior to filing. M.P.E.P. at § 2164.02, *citing Gould v. Quigg*, 822 F.2d 1074, 3 U.S.P.Q.2d 1302 (Fed. Cir. 1987). "The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation." *Id.* In this case, however, the

specification contains examples of at least three different examples of the claimed compositions: peptides, chimeric proteins, and antibodies.

It is well established law that the claims should be interpreted in view of the specification - in this case, the extensive disclosure in the specification at pages 11 and 13-27, which describes molecules including proteins, antibodies, compounds identified using combinatorial, and compounds identified by rational drug design, using the guidelines provided based on the discovery that one short peptide sequence of human CD59 alone is responsible for the species-specific binding of CD59 to inhibit formation of the C5-b9 complex, using the standard of one skilled in the art.

With computer programs that can be downloaded readily from the internet, and the entire amino acid sequences of the relevant molecules (CD59 and C9) being known, it would be routine to create a three dimensional structure as claimed. The invention resides in knowing which portion of these two structures are critical for species-specific binding, not in how to make a molecule or screen for the molecule, once the underlying structure is known. The examiner's statement that "It would require undue experimentation to investige **all** such "molecules" is legally incorrect - the standard is not whether one can make **all** such molecules, but whether one can make molecules necessary to practice the claimed method. This standard has been met. The examiner has cited no factual support, no literature support and no data that demonstrates anything to the contrary or that appellants' statements are not correct.

(iii) Rejections Under 35 U.S.C. § 112, second pararaph

As the Board is aware the standard for enablement and clarity is what one of skill in the art, would understand from the claims in view of the specification. Those skilled in

the art would learn from the extensive examples that a very small region of human CD59 is responsible for CD59 species-specific role as a complement inhibitor. Indeed, the data at page 47 shows just how specific this role is, since substitution of amino acids to create the structure present in the analogous region of rabbit CD59 destroys the ability of the molecule to inhibit C5b-9 complex formation. The computer programs available at the time of filing provide extensive guidance once the data regarding the exact composition and spatial orientation and alignment provided by applicants has been entered into the program. Moreover, the assays can be used as a final determining factor – since the requirements for inhibition are so stringent, failure to inhibit formation of the human C5b-9 complex can be used as a rapid, simple screen. The requirement of a specific functional activity has been incorporated into the independent claim.

The examiner has stated that appellant should amend the claims to define an antibody binding to C9, rather than a peptidomimetic which mimicks the structure of CD59 amino acids 42-58. This however, is not appellants' invention: the invention is the discovery that the structure of amino acids 42-58 is what is responsible for binding to C9 in a species-specific manner. *Most,* if not all, known antibodies to C9 are not species-specific. A priori, they must be different from, and cannot have the structure of, human CD59 amino acids 42-58. Indeed, as described in the application, the most likely way to make a suitable antibody is to make an anti-ID antibody, that is, an antibody to an antibody specifically reactive with amino acids 42-58 of human CD59. An antibody made to C9 which have a structure complementary to the C9 amino acid residues; not mimicking amino acid sequence of human CD59.

(iv) Rejections Under 35 U.S.C. § 102

Claim 10 is drawn to a method for inhibiting human C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition comprising a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules having the structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9.

Sims does not identify CD amino acid residues 42-59 nor that this region binds to amino acid residues 359-384, either explicitly nor implicitly. This fact simply was not known until the studies described in this application were performed. It is not enough to stay that because antibodies which bind to CD59, or C9, are disclosed, that these antibodies are specific for these regions.

Sims et al. is based on the discovery that CD59 inhibits complement activation, not just hemolysis, and notes that antibodies to C9 can be used to inhibit CD59 activity. There is no disclosure of what region of CD59 imparts species-specificity. Merely because there may be an antibody which binds to C9 does not mean that it mimicks the region of CD59 which is in issue; in fact, absent making the antibody by immunization with this region, and then making an anti-ID antibody to the antibody to the human CD59, one would instead only have an antibody to C9, not an antibody mimicking structure of human CD59. Accordingly, Sims does not disclose nor make obvious the claimed subject matter.

(v) Rejections Under 35 U.S.C. § 103

As discussed above, Sims fails to disclose the critical region of human CD59 which must be imitated, and the region of human C9 which is bound by this species specific portion of CD59, which is essential for design and use of inhibitors of the species specific reaction between human CD59 and human C9. The structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9, is simply not taught by Sims, therefore one skilled in the art would not be led to make inhibitors based on their sequence and structure. Sims actually teaches away from what is claimed, by focusing on C9 sequence, not CD59 sequence!

Chang is of no assistance in this regard. Chang identifies the region of human C9 which is bound by human CD59; not the portion of CD59 which binds. One cannot extrapolate from the information relating to human C9 to obtain information about human CD59. The identification of the critical amino acid sequence required careful analysis and many experiments, as discussed above. Absent this information, one cannot make antibodies to this region of CD59; one cannot design peptide mimics of this region of CD59; one cannot design protein chimeras of this region of CD59.

The requirement for binding to a specific region of C9 is a specific limitation of the claimed compounds, as is the need to mimick the structure of a specific region of human CD59. There is simply no teaching in the art which discloses nor leads one to these limitations, nor is it obvious. Only through careful, repetitive, and exacting studies was it possible to determine which amino acid residues were critical to block **species specific binding,** which is essential if one is to then make a compound not only binding to the C9 target but mimicking the structure of the human CD59.

The examiner's insistence that the claim language should be re-written to define the claimed invention as an anti-C9 antibody is simply additional evidence that what is claimed is **not** the same as what is described in the prior art - it is in fact the opposite of what is claimed. Again, an antibody to C9 will have a structure complementary to the C9 amino acid epitope; what is claimed is a compound having a structure which mimicks human CD59 sequence, indeed, a very short, specific sequence. These are neither the same nor are they obvious from each other.

(9) SUMMARY AND CONCLUSIONS

Claims 10-17, at a minimum, and more properly claims 10-17, 27-29 and 33-35, should be allowed as enabled, definite, and novel and non-obvious over the prior art.

None of the art discloses nor makes obvious the claimed compound which inhibits formation of the human C5b-9 complex, by imitating the structure and function of amino acid residues 42-58. The claims are both definite and enabled. Therefore claims 10-17 should be allowed and the case remanded to the examiner for consideration of claims 10-17, 27-29, and 33-35 on the merits as to all species.

Respectfully submitted,

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Date: June 26, 2002
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CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this Reply to Examiner's Answer, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: June 26, 2002

Pam Turnbough

APPENDIX : CLAIMS ON APPEAL

1. A compound that specifically inhibits the formation of the hu C5b-9 complex selected from the group consisting of molecules structurally mimicking CD59 amino acid residues 42 to 58 when they are in a spatial orientation which inhibits formation of the hu C5b-9 complex, wherein the compound is not hu CD59.

2. The compound of claim 1, selected from the group consisting of proteins, peptides, nucleic acids, and small molecules which bind specifically to amino acids 359 to 384 of hu C9.

3. The compound of claim 2, wherein the protein is an antibody.

4. The compound of claim 2, wherein the protein is a chimeric peptide which includes the amino acids 42 to 58 of the human sequence of CD59.

5. The compound of claim 2, wherein the peptide is a covalently cyclized peptide comprising hu CD59 amino acid residues 42 to 58.

6. The compound of claim 2, wherein the composition is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of hu CD59.

7. The compound of claim 1, further comprising a pharmaceutically acceptable carrier for administration to patients in need thereof.

8. The compound of claim 1 wherein the compound is a peptidomimetic compound comprising the side chains of hu CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in an equivalent spacial orientation and alignment to that presented on the surface of hu CD59.

9. The compound of claim 8 wherein the spacial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are

equivalent to the spacial orientation and alignment deduced by NMR structure determination.

10. A method for inhibiting human C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition comprising a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules having the structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9.

11. The method of claim 10, wherein the peptidomimetic is a small molecule which binds specifically to amino acids 359 to 384 of human C9.

12. The method of claim 10, wherein the protein is an antibody.

13. The method of claim 10, wherein the protein is a chimeric peptide which includes the amino acids 42 to 58 of the human sequence of CD59.

14. The method of claim 10, wherein the peptide is a covalently cyclized peptide comprising human CD59 amino acid residues 42 to 58.

15. The method of claim 10, wherein the peptidomimetic is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of human CD59.

16. The method of claim 10, wherein the composition further comprises a pharmaceutically acceptable carrier for administration to patients in need thereof.

17. The method of claim 10, wherein the patient is in need of suppression of complement-mediated inflammation.

18. The method of claim 10 wherein the peptidomimetic comprises the side chains of human CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the spatial orientation and alignment of hu CD59.

19. The method of claim 18 wherein the spatial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are deduced by NMR structure determination.

20. A compound that specifically promotes the formation of the hu C5b-9 complex selected from the group consisting of molecules structurally mimicking C9 amino acid residues 359 to 384 when they are in a spatial orientation which promotes formation of the C5b-9 complex, wherein the compound is not hu C9.

21. The compound of claim 20, selected from the group consisting of proteins, peptides, nucleic acids, and small molecules which bind specifically to amino acids 42 to 58 of hu CD59.

22. The compound of claim 21, wherein the protein is an antibody.

23. The compound of claim 21, wherein the protein is a chimeric peptide which includes the amino acids 359 to 384 of the human sequence of C9.

24. The compound of claim 21, wherein the peptide is a covalently cyclized peptide comprising hu C9 amino acid residues 359 to 384.

25. The compound of claim 21, wherein the composition is a peptide of less than forty amino acids residues including amino acid residues 359 to 384 of hu C9.

26. The compound of claim 20, further comprising a pharmaceutically acceptable carrier for administration to patients in need thereof.

27. A method for specifically promoting hu C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition to decrease CD59 inhibition of C5b-9 complex assembly wherein the composition comprises a compound selected from the group consisting of molecules structurally mimicking C9 amino acid residues 359 to 384 when they are in a spatial orientation which promotes formation of the complex, wherein the compound is not hu C9.

28. The method of claim 27, wherein the compound is selected from the group consisting of proteins, peptides, nucleic acids, and small molecules which bind specifically to amino acids 42 to 58 of hu CD59.

29. The method of claim 28, wherein the protein is an antibody.

30. The method of claim 28, wherein the protein is a chimeric peptide which include the amino acids 359 to 384 of the human sequence of C9.

31. The method of claim 28, wherein the peptide is a covalently cyclized peptide comprising hu C9 amino acid residues 359 to 384.

32. The method of claim 28, wherein the composition is a peptide of less than forty amino acids residues including amino acid residues 359 to 384 of hu C9.

33. The method of claim 27, wherein the composition further comprises a pharmaceutically acceptable carrier for administration to patients in need thereof.

34. The method of claim 27, wherein the patient is in need of complement activation.

35. The method of claim 27, wherein the composition is administered as a adjunct to tumor therapy.

#29 GD

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Peter J. Sims

Serial No: 09/020,393 Art Unit: 1644

Filed: February 9, 1998 Examiner: Gambel, P.

For: *COMPOSITIONS AND METHODS TO INHIBIT FORMATION OF THE C5B-9 COMPLEX OF COMPLEMENT*

Commissioner of Patents and Trademarks
Washington, D.C. 20231

REQUEST FOR ORAL HEARING

Sir:

Pursuant to 37 C.F.R. § 1.194, Appellant respectfully requests an oral hearing in the Appeal to the Board of Appeals from the Office Action mailed April 26, 2002, finally rejecting claims 10-12 and 16-17, and the Examiner's Answer mailed April 26, 2002, in the above-identified application.

Also enclosed is a check in the amount of $140.00, the fee for filing a Request for Oral Hearing before the Board of Patent Appeals and Interferences, by a small entity as specified in 37 C.F.R. § 1.17(d). It is believed that no other fee is required. However, should a fee be required, the Commissioner is hereby authorized to charge any additional fee, or credit any

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overpayment in connection with this matter, to Deposit Order Account No. 50-1868.

To facilitate this process, a duplicate of this Request for Oral Hearing is enclosed.

Respectfully submitted,

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Reg. No. 31,284

Date: June 26, 2002

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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)

I hereby certify that this REQUEST FOR ORAL HEARING and any paper referred to as being attached or enclosed, are being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to Commissioner for Patents, Washington, D.C. 20231.

Pam Turnbough

Pam Turnbough

Date: June 26, 2002

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